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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/049,696	03/27/98	BILLING-MEDEL	P 6067.US.01

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EXAMINER	
KERR, J	

ART UNIT	PAPER NUMBER
1633	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/049,696	Applicant(s) Billing-Medel et al.
	Examiner Janet M. Kerr	Group Art Unit 1633

☒ Responsive to communication(s) filed on *Nov 17, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-18* is/are pending in the application.

Of the above, claim(s) *7-10, 12-14, and 16* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 11, 15, 17, and 18* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-18 are pending.

Applicant's election of Group I in Paper Nos. 6 and 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 7-10, 12-14, and 16 are withdrawn from further consideration by the examiner as being drawn to a non-elected.

Claims 1-6, 11, 15, 17, and 18 are being examined on the merits.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the section under Claim to benefit of earlier U.S. application(s) under 35 U.S.C. 120 indicates that there are no earlier applications to which Applicants are claiming priority. However, on page 1 of the specification, under "Cross-Reference to Related Application", priority to U.S. application Serial No. 08/829,754 is claimed. A new declaration is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 15, 17, and 18 are rejected under 35 U.S.C. § 101 as being drawn to nonstatutory subject matter. As written, claim 15 is drawn to an organism or cell, *per se*, which is a product of nature, and therefore not patentable under 35 U.S.C. § 101. It is suggested that applicants use

the language "purified" in connection with the CS194 polynucleotide or fragment thereof to identify a product that is not found in nature. Similarly, claims 17 and 18 read on products of nature, and are therefore not patentable under 35 U.S.C. § 101. It is suggested that applicants use the language "purified" in connection with the gene or fragment thereof to identify a product that is not found in nature.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. See Interim guidelines for the requirement for Written Description as cited in the Federal Register, Vol. 63, No. 114, p. 3263.

The claims are directed to purified polynucleotides or fragments thereof derived from a CS194 gene. As written, the claims encompass polynucleotides comprising non-disclosed nucleic acid sequences attached to the claimed SEQ ID NOS. When given its broadest reasonable interpretation, the claims encompasses genes containing the nucleotide sequences of SEQ ID NOS. 1-20, or genes encoding the protein sequence as set forth in SEQ ID NO. 41. However, there is no disclosure in the specification of genomic sequences which comprise nucleic acids associated with the claimed polynucleotides.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In this case, the elected SEQ ID Nos. are the only species whose complete structure is disclosed. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence). Possible identifying characteristics could include size of the polynucleotide, the location to which it maps in the genome, restriction maps, biological activity of the encoded product, etc. No such identifying characteristics are provided for any polynucleotide. While applicants were obviously in possession of the nucleic acid sequences as set forth in the disclosed SEQ ID NOS., the specification provides no information regarding sequences which are naturally attached to the claimed nucleic acid sequences, i.e., nucleic acid sequences comprising 5' regulatory regions or introns. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of polynucleotides besides the claimed SEQ ID NOS., at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genera.

In addition, claims 4 and 11 are directed to polynucleotides which comprise a sequence encoding at least one CS194 epitope. The specification defines the term "epitope" as an antigenic determinant of a polypeptide or protein. The epitope can comprise three amino acids in a spatial conformation which is unique to the epitope. Alternatively, the epitope can consist of at least five such amino acids and more usually, or the epitope can consist of at least eight to ten amino acids. A "conformational epitope" is defined as an epitope that is comprised of a specific juxtaposition of amino acids in an immunologically recognizable structure, such amino acids being present on the same polypeptide in a contiguous or non-contiguous order or present on different polypeptides (see, e.g., page 16, lines 3-31 of the specification). However, the specification fails to disclose any particular sequence which may encode an epitope, nor does the specification identify nucleic acid sequences encoding three, five or eight to ten amino acids which are antigenic determinants. The limited information provided in the specification is not deemed sufficient to

reasonably convey to one skilled in the art that applicants were in possession of polynucleotides encoding epitopes, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for polynucleotides or fragments thereof encoding CS194 epitopes.

Enablement

Claims 1-6, 11, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid sequences set forth in the claimed SEQ ID NOS., does not reasonably provide enablement for nucleic acid sequences which are capable of selectively hybridizing to the nucleic acid of the CS194 gene and which have at least 50% identity with a sequence selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof. In addition, the specification does not reasonably provide enablement for nucleic acid sequences which encode epitopes of CS194. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to polynucleotides or fragments thereof obtained from a CS194 gene, wherein the polynucleotides are capable of selectively hybridizing to the nucleic acid of the CS194 gene and wherein the polynucleotides have at least 50% identity with a sequence selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof. As written, the claims embrace polynucleotides containing sequences adjacent in nature, i.e., 5' regulatory sequences and intronic sequences.

The instant specification is directed to the preparation and sequence characterization of particular polynucleotides that are disclosed. The claimed SEQ ID NOS. represent fragments or overlapping sequences of cDNA clones prepared using the methods disclosed in the specification. However, these are the only polynucleotides whose sequences are disclosed. The specification

does not disclose a CS194 gene *per se*, nor does the specification provide an example of the genomic structure of CS194, nor methods, including the necessary reagents, which would be used to specifically isolate the gene. In view of the lack of an example of the genomic structure of the CS194 gene, or sequences comprising 5' regulatory regions or intronic regions of the CS194 gene, and in view of the lack of guidance as to the methods and reagents required for isolating the gene, one of ordinary skill in the art would not have had a high expectation of successfully isolating a CS194 gene without undue experimentation. Moreover, the claims are directed to fragments of the disclosed polynucleotides. However, the specification does not provide guidance as to how to select the fragments, the size of the fragments, or how any particular fragment is to be used. Therefore, given that the specification fails to teach how one would prepare portions of the specifically disclosed sequences that would be useful for any particular function with any particular specificity, the artisan would be required to exercise undue experimentation in the preparation and use of portions of the particularly disclosed polynucleotides. Consequently, limitation of the scope of the claims to the specific sequences referred to by SEQ ID No. is appropriate.

With regard to the limitation that the polynucleotides or fragments thereof are capable of selectively hybridizing to the nucleic acid of the CS194 gene, and wherein the polynucleotides or fragments thereof have at least 50% identity with a sequence selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof, it should be noted that the specification does not teach a specific algorithm or parameters required to calculate the claimed sequence identity. For example, the necessary parameters required to calculate the claimed sequence identity, using a disclosed, given algorithm, include gap penalties and mismatch penalties. As percent identity may vary depending upon how gaps, substitutions, and sequences of unequal length are scored, one of ordinary skill in the art would not have been able to make any particular DNA sequence at less than 100% identity without undue experimentation.

Similarly, with regard to the limitation that the polynucleotides selectively hybridize to the nucleic acid of the CS194 gene, the specification fails to provide adequate guidance as to which

hybridization conditions are required such that all of the polynucleotides and fragments thereof embraced by the claims selectively hybridize to the nucleic acids set forth in SEQ ID NOS. 1-20 or fragments thereof. Nucleic acid hybridization assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it would require undue experimentation for one of ordinary skill in the art to ascertain the hybridization conditions such that all of the claimed polynucleotides and fragments thereof would be capable of selectively hybridizing to the polynucleotides of SEQ ID NOS. 1-20 and fragments thereof. For example, Carrico (US Patent No. 5,200,313) discloses factors which affect hybridization reactions including:

1. The purity of the nucleic acid preparation.

2. Base compositions of the probe - G-C base pairs will exhibit greater thermal stability than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.

3. Length of homologous base sequences- Any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.

4. Ionic strength- The rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.

5. Incubation temperature- Optimal reannealing occurs at a temperature about 25 - 30 C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.

6. Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.

7. Denaturing reagents- The presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.

8. Incubation- The longer the incubation time, the more complete will be the hybridization.

9. Volume exclusion agents- The presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

10. Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic strength, and increasing temperature, e.g., 0.1X SSC for 30 minutes at 65 C, will, with increasing effectiveness, remove non-fully complementary hybridization products.

Given the numerous variables which impact on the capability of a polynucleotide to hybridize to any other polynucleotide, and given the lack of guidance in the specification as to which hybridization conditions are required such that "specific hybridization" can occur, one of ordinary skill in the art would not have had a high expectation of successfully obtaining the claimed polynucleotides without undue experimentation.

With regard to claims 4 and 11, which are directed to polynucleotides which comprise a sequence encoding at least one CS194 epitope, the specification does not provide any specific example of a CS194 epitope, nor does the specification provide guidance as to how one of ordinary skill in the art would select an appropriate

polynucleotide sequence encoding an amino acid sequence which functions as an epitope. As discussed in the above "Written Description" rejection, the specification defines the term "epitope" as an antigenic determinant of a polypeptide or protein. The epitope can comprise three amino acids in a spatial conformation which is unique to the epitope. Alternatively, the epitope can consist of at least five such amino acids and more usually, or the epitope can consist of at least eight to ten amino acids. A "conformational epitope" is defined as an epitope that is comprised of a specific juxtaposition of amino acids in an immunologically recognizable structure, such amino acids being present on the same polypeptide in a contiguous or non-contiguous order or present on different polypeptides (see, e.g., page 16, lines 3-31 of the specification). However, the specification fails to disclose any particular sequence which may be deemed an epitope, nor does the specification identify nucleic acid sequences encoding three, five or eight to ten amino acids which are antigenic determinants. Moreover, while the specification discloses that the nucleotide sequences contain open reading frames from which an immunogenic epitope may be found, and that such an epitope is believed to be unique to the disease state or condition associated with CS194, the specification does not disclose any epitope which is unique to a disease state or condition associated with CS194. Thus, absent examples of specific epitopes, and in view of the lack of guidance in the specification as to how to select the nucleic acid sequences which would encode suitable epitopes, one of ordinary skill in the art would not have had a high expectation of successfully and reproducibly determining the appropriate nucleic acid sequences to use in generating CS194 epitopes without undue experimentation.

Taken together, the full scope of the claims is not enabled because of the large number of sequences embraced by the claims coupled with the lack of adequate guidance in the application as to which sequences to isolate or construct. Thus, one of skill in the art would need to perform undue experimentation to practice the full scope of the claims. The Court of Appeals for the Federal Circuit has ruled that claims that embrace a large

number of species of polynucleotide sequences without proper guidance in the application as to how to make and use such polynucleotides do not meet the requirements of 35 U.S.C. § 112, first paragraph, *Amgen v. Chugai* (18 USPQ2d 1016 (Fed. Cir. 1991)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite for the following reasons; the phrase "is capable of selectively hybridizing to the nucleic acid of said CS194 gene" is indefinite because it is unclear what conditions are necessary such that the polynucleotide or fragment thereof has the capability of selective hybridization, moreover, as "selective" is a relative term which has not been defined in the claim or the specification, it is unclear how the hybridization is "selective". The metes and bounds of the phrases are unclear.

Claims 1 and 5 are rendered vague and indefinite by the phrase "derived from" as it is unclear how an open reading frame can be derived from "CS194". In addition, it is unclear if the usage of the term "CS194" in claim 5 is similar to that of claim 1, i.e., does the term CS194 represent a specific nucleic acid sequence or does CS194 represent some other molecule?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3, 5, 6, 15, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Yu *et al.* (U.S. Patent No. 5,733,748, 1998, filing date 6/6/95).

Yu *et al.* disclose and claim the isolated polynucleotide of Seq. ID. No. 8. (see, e.g., columns 39-42, and claims 15 and 17) which corresponds to the same nucleic acid sequences of Seq I.D. Nos. 12-20 as follows (see also the attached nucleic acid comparison results):

Instant Application		Patent: SEQ ID NO 8
SEQ ID NO.	Nucleic Acids	Nucleic Acids
SEQ ID NO 12	171-235	1-65
SEQ ID NO 13	1-227	56-282
SEQ ID NO 14	1-248	306-553
SEQ ID NO 15	1-154	545-699
SEQ ID NO 16	1-213	625-837
SEQ ID NO 17	1-89	717-805
SEQ ID NO 18	1992-2676	1-685
SEQ ID NO 19	692-1528	1-837
SEQ ID NO 20	1992-2828	1-837

As the sequence of Yu *et al.* has at least 50% identity with a sequence selected from SEQ ID Nos. 12-20, the sequence of Yu *et al.* has an open reading frame and will hybridize to a nucleic acid sequence of CS194 absent evidence to the contrary. Moreover, Yu *et al.* disclose that the sequence can be recombinant or synthetic, that the sequence can be included in an expression

vector operatively linked to an appropriate expression control sequence, and that the vector containing the polynucleotide can be introduced into an appropriate host cell (see, e.g., column 4, lines 62-67, and column 13, lines 1-32).

Thus, as Yu *et al.* disclose the claimed recombinant and synthetic nucleic acid sequences, vectors comprising the nucleic acid sequences and host cells comprising the vectors, the disclosure of Yu *et al.* anticipates the claimed invention.

Claims 1, 2, 5, 6, 15, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Cunningham *et al.* (J. Biol. Chem., 270:52, 31016-31026, 1995).

Cunningham *et al.* disclose isolated polynucleotides which have at least 50% identity with a sequence selected from SEQ ID Nos. 1-20 as follows (see Figure 1 on pages 31018-31019 of the reference and also the attached nucleic acid comparison results):

SEQ ID NO.	Location in Reference	Location in Prior Art SEQ	Location in claimed SEQ ID NO.
SEQ ID NO 1	"origin"	7-214	13-223
SEQ ID NO 2	"origin"	125-395	2-272
SEQ ID NO 3	"origin"	317-550	4-237
SEQ ID NO 4	"origin"	645-819	7-181
SEQ ID NO 5	"origin"	752-977	1-220
SEQ ID NO 6	"origin"	934-1184	1-251
SEQ ID NO 7	"origin"	1465-1502	11-288
SEQ ID NO 8	"origin"	1304-1550	1-253
SEQ ID NO 9	"origin"	1417-1629	5-217
SEQ ID NO 10	"origin"	1531-1737	1-198
SEQ ID NO 11	"origin"	1687-1841	37-182

SEQ ID NO 12	"origin"	1847-2069	11-233
SEQ ID NO 13	"origin"	2062-2274	1-213
SEQ ID NO 14	"origin"	2337-2549	29-241
SEQ ID NO 15	"origin"	2548-2637	1-90
SEQ ID NO 18	"origin"	7-2637	13-2625
SEQ ID NO 19	"origin"	1304-2637	1-1325
SEQ ID NO 20	"origin"	7-2637	13-2625

As the polynucleotide of Cunningham *et al.* has at least 50% identity with a sequence selected from SEQ ID Nos. 12-20, the polynucleotide sequence of Cunningham *et al.* will necessarily hybridize to the nucleic acid sequence of CS194 absent evidence to the contrary. Moreover, Cunningham *et al.* disclose that the polynucleotide is inserted into an expression vector operatively linked to an appropriate expression control sequence, and that the vector containing the polynucleotide is introduced into a host cell (see, e.g., page 31017, under "Methods").

Thus, as Cunningham *et al.* disclose the claimed recombinant nucleic acid sequences, vectors comprising the nucleic acid sequences and host cells comprising the vectors, the disclosure of Cunningham *et al.* anticipates the claimed invention.

Thus, the disclosure of Cunningham *et al.* anticipates the claimed polynucleotides.

Claims 1, 2, 15, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Okubo *et al.*, (GenBank Acc. No. D25727, 1995).

Okuba *et al.* disclose isolated polynucleotides which have at least 50% identity with a sequence selected from SEQ ID Nos. 15-18 and 20 as follows (see also the attached nucleic acid comparison results):

SEQ ID NO.	Location in Reference	Location in Prior Art SEQ	Location in claimed

			SEQ ID NO.
SEQ ID NO 15	"origin"	1-115	40-154
SEQ ID NO 16	"origin"	43-254	2-213
SEQ ID NO 17	"origin"	133-238	1-106
SEQ ID NO 18	"origin"	49-212	2623-2786
SEQ ID NO 20	"origin"	49-212	2623-2786

As the sequences of Okuba *et al.* have at least 50% identity with a sequence selected from SEQ ID Nos. 15-18 and 20, the nucleic acid sequences of Okuba *et al.* will necessarily hybridize to the nucleic acid sequence of CS194 absent evidence to the contrary.

Thus, the disclosure of Okuba *et al.* anticipates the claimed polynucleotides.

Claims 1-3, 5, 6, 15, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by:

Hillier *et al.*, GenBank Acc. No. R28408, 1995, with respect to SEQ ID NO. 1;
Hillier *et al.*, GenBank Acc. No. H10546, 1995, with respect to SEQ ID NO. 2;
Hillier *et al.*, GenBank Acc. No. H10546, 1995, with respect to SEQ ID NO. 3;
Waterston *et al.*, GenBank Acc. No. M75917, 1992, with respect to SEQ ID NO. 4;
Waterston *et al.*, GenBank Acc. No. M75917, 1992, with respect to SEQ ID NO. 5;
Hillier *et al.*, GenBank Acc. No. H57955, 1995, with respect to SEQ ID NO. 6;
Hillier *et al.*, GenBank Acc. No. H52536, 1995, with respect to SEQ ID NO. 7;
Hillier *et al.*, GenBank Acc. No. H52536, 1995, with respect to SEQ ID NO. 8;
Burnett *et al.*, GenBank Acc. No. Q51025, 1994, with respect to SEQ ID NO. 9;
Hillier *et al.*, GenBank Acc. No. R79129, 1995, with respect to SEQ ID NO. 10;
Hillier *et al.*, GenBank Acc. No. R79129, 1995, with respect to SEQ ID NO. 11;
Hillier *et al.*, GenBank Acc. No. R55449, 1995, with respect to SEQ ID NO. 12;

Kohara *et al.*, GenBank Acc. No. D27036, 1995, with respect to SEQ ID NO. 13;
Hillier *et al.*, GenBank Acc. No. R72678, 1995, with respect to SEQ ID NO. 14;
Hillier *et al.*, GenBank Acc. No. R51322, 1995, with respect to SEQ ID NO. 15.

This rejection applies insofar as the claims are deemed to embrace polynucleotides that have at least 50% identity with a sequence selected from the group consisting of SEQ ID Nos 1-15, and fragments or complements thereof. Each of the references discloses a fragment that has at least 50% identity with a fragment or complement of the claimed SEQ ID Nos. The locations of these fragments are shown in the table below. Since each of the references discloses a common sequence (or its complement) with one of the claimed SEQ ID Nos., each of the references discloses a polynucleotide that is embraced by the claims. Additionally, each of the references discloses recombinant nucleic acids and vectors that contain the polynucleotides embraced by the polynucleotide claims.

SEQ ID NO.	Reference	Location in Reference	Location in Prior Art SEQ	Location in claimed SEQ ID NO.
1	Hillier *et al.*	"Origin"	36-20	58-74
2	Hillier *et al.*	"Origin"	351-368	233-250
3	Hillier *et al.*	"Origin"	351-369	43-61
4	Waterston *et al.*	"Origin"	57-41	120-136
5	Waterston *et al.*	"Origin"	57-41	7-23
6	Hillier *et al.*	"Origin"	143-127	223-239

7	Hillier *et al.*	"Origin"	62-79	147-164
8	Hillier *et al.*	"Origin"	62-79	64-81
9	Burnett *et al.*	"Origin"	1688-1703	113-128
10	Hillier *et al.*	"Origin"	6-22	124-140
11	Hillier *et al.*	"Origin"	6-22	13-29
12	Hillier *et al.*	"Origin"	38-54	200-216
13	Kohara *et al.*	"Origin"	245-229	134-150
14	Hillier *et al.*	"Origin"	369-387	60-78
15	Hillier *et al.*	"Origin"	44-60	51-67

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the

examiner be unavailable, inquiries should be directed to John LeGuyader, Supervisory Primary Examiner, at (703) 308-0447. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600

JOHN L. LeGUYADER
PRIMARY EXAMINER
GROUP 1600
1600